

What is claimed is:

1. An aqueous composition comprising condensed plasmid DNA and a carrier, wherein the carrier comprises a lyophilizable, water-miscible alcohol and a divalent cation.
- 5 2. The composition of claim 1, wherein the lyophilizable water-miscible alcohol is tert-butanol.
3. The composition of claim 2, wherein the concentration of tert-butanol is from about 15% to about 35% by volume.
- 10 4. The composition of claim 3, wherein the concentration of tert-butanol is from about 17% to about 25% by volume.
5. The composition of claim 4, wherein the concentration of tert-butanol is about 20% by volume.
- 15 6. The composition of claim 1, wherein the divalent cation is selected from the group consisting of Ca^{+2} , Mg^{+2} or Zn^{+2} .
- 20 7. The composition of claim 6, wherein the divalent cation is Ca^{+2} .
8. The composition of claim 7, wherein the concentration of Ca^{+2} is from about 0.2 to about 2 millimolar.
- 25 9. The composition of claim 8, wherein the concentration of Ca^{+2} is about 1 millimolar.
10. The composition of claim 9, wherein the concentration of DNA is from about 10 ug/mL to about 200 ug/mL.
- 30 11. The composition of claim 10, wherein the molar ratio of Ca^{+2} to DNA-phosphate is about 3.
12. The composition of claim 10, wherein the concentration of Ca^{+2} in millimolar units, is about $16 \cdot e^{(0.1386 \cdot t)}$, wherein t is the volume-percent of *tert*-butanol, and the counterion to the Ca^{+2} is chloride, and wherein the concentration of tert-butanol is from about 15% to about 35% by volume.
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13. The composition of claim 1, wherein the counterion to the divalent cation is chloride.
14. The composition of claim 1, wherein the DNA has a negative zeta potential.
15. The composition of claim 1, wherein the DNA is stable to shear stress.
16. The composition of claim 15, wherein the shear stress is sonication-induced.
17. The composition of claim 15, wherein the plasmid DNA remains intact following sonication for 60 seconds using a 50 watt probe sonicator.
18. The composition of claim 17, wherein the total percent of supercoiled, open circular and linear plasmid DNA together after sonication is greater than 90% of its initial value.
19. The composition of claim 1, wherein the DNA in the condensate consists essentially of toroids, rods and spheres.
20. The composition of claim 19, wherein the toroids exhibit a median particle size in the range of from about 50 to about 100 nanometers, as measured by electron microscopy.
21. The composition of claim 1, wherein the condensate exhibits a bimodal particle size distribution.
22. The composition of claim 21, wherein the particle size distribution of the condensate, measured by dynamic light scattering, exhibits peaks in the range of from about 40 to about 70 nanometers and from about 200 to about 500 nanometers.
23. A method to condense plasmid DNA comprising:
(a) preparing an aqueous solution of deionized plasmid DNA;
(b) adding a lyophilizable, water-miscible alcohol to the solution of step (a);
and
(c) adding a divalent cation to the mixture of step (b).
24. The method of claim 23, wherein the lyophilizable water-miscible alcohol is tert-butanol.

25. The method of claim 24, wherein the concentration of tert-butanol is from about 15% to about 35% by volume.

5 26. The method of claim 25, wherein the concentration of tert-butanol is from about 17% to about 25% by volume.

27. The method of claim 26, wherein the concentration of tert-butanol is about 20% by volume.

10 28. The method of claim 23, wherein the divalent cation is selected from the group consisting of Ca^{+2} , Mg^{+2} or Zn^{+2} .

29. The method of claim 28, wherein the divalent cation is Ca^{+2} .

15 30. The method of claim 29, wherein the concentration of Ca^{+2} is from about 0.2 to about 2 millimolar.

31. The method of claim 30, wherein the concentration of Ca^{+2} is about 1 millimolar.

20 32. The method of claim 31, wherein the concentration of DNA is from about 20 ug/mL to about 200 ug/mL.

25 33. The method of claim 32, wherein the molar ratio of Ca^{+2} to DNA-phosphate is about 3.

34. The method of claim 29, wherein the concentration of Ca^{+2} in millimolar units, is about $16 \cdot e^{(0.1386 \cdot t)}$, wherein t is the volume-percent of *tert*-butanol, and the counterion to the Ca^{+2} is chloride, and wherein the concentration of tert-butanol is from about 15% to about 30 35% by volume.

35 35. The method of claim 23, wherein the counterion to the divalent cation is chloride.

36. The method of claim 23, wherein the DNA has a negative zeta potential.

37. The method of claim 23, which further comprises removing water and the lyophilizable, water-miscible alcohol from the composition.

38. The method of claim 37, wherein the water and the lyophilizable, water-miscible alcohol are removed by lyophilization.
39. The method of claim 37 which further comprises spray-drying the composition.
40. A composition prepared according to claim 35.
41. A method of protecting DNA against shear stress comprising:
(a) preparing an aqueous solution of deionized plasmid DNA;
(b) adding a lyophilizable, water-miscible alcohol to the solution of step (a);
and
(c) adding a divalent cation to the mixture of step (b).
42. The method of claim 41, wherein said shear stress is sonication-induced.
43. The method of claim 41, wherein the lyophilizable water-miscible alcohol is tert-butanol.
44. The method of claim 43, wherein the concentration of tert-butanol is from about 15% to about 35% by volume.
45. The method of claim 44, wherein the concentration of tert-butanol is from about 17% to about 25% by volume.
46. The method of claim 45, wherein the concentration of tert-butanol is about 20% by volume.
47. The method of claim 41, wherein the divalent cation is selected from the group consisting of Ca^{+2} , Mg^{+2} or Zn^{+2} .
48. The method of claim 47, wherein the divalent cation is Ca^{+2} .
49. The method of claim 48, wherein the concentration of Ca^{+2} is from about 0.2 to about 2 millimolar.
50. The method of claim 47, wherein the concentration of Ca^{+2} is about 1 millimolar.

51. The method of claim 50, wherein the concentration of DNA is from about 10 ug/mL to about 200 ug/mL.

52. The method of claim 51, wherein the molar ratio of Ca^{+2} to DNA-phosphate is about 3.

53. The method of claim 49, wherein the concentration of Ca^{+2} in millimolar units, is about $16 \cdot e^{(0.1386 \cdot t)}$, wherein t is the volume-percent of *tert*-butanol, and the counterion to the Ca^{+2} is chloride, and wherein the concentration of *tert*-butanol is from about 15% to about 35% by volume.

54. The method of claim 41, wherein the counterion to the divalent cation is chloride.

55. The method of claim 41, wherein the DNA has a negative zeta-potential.

56. The method of claim 41, which further comprises removing water and the lyophilizable, water-miscible alcohol from the composition.

57. The method of claim 56, wherein the water and the lyophilizable, water-miscible alcohol are removed by lyophilization.

58. The method of claim 55 which further comprises spray-drying the composition.

59. A method for preparing a DNA condensate comprising:
 (a) preparing an aqueous solution of deionized plasmid DNA;
 (b) adding a lyophilizable, water-miscible alcohol to the solution of step (a);
 and
 (c) adding a divalent cation to the mixture of step (b),
 wherein said DNA condensate consists essentially of toroids, rods and spheres.

60. The method of claim 59, wherein the lyophilizable water-miscible alcohol is *tert*-butanol.

61. The method of claim 60, wherein the concentration of *tert*-butanol is from about 15% to about 35% by volume.

62. The method of claim 61, wherein the concentration of tert-butanol is from about 17% to about 25% by volume.

5 63. The method of claim 62, wherein the concentration of tert-butanol is about 20% by volume.

64. The method of claim 59, wherein the divalent cation is selected from the group consisting of Ca^{+2} , Mg^{+2} or Zn^{+2} .

10 65. The method of claim 64, wherein the divalent cation is Ca^{+2} .

66. The method of claim 65, wherein the concentration of Ca^{+2} is from about 0.2 to about 2 millimolar.

15 67. The method of claim 66, wherein the concentration of Ca^{+2} is about 1 millimolar.

68. The method of claim 67, wherein the concentration of DNA is from about 20 ug/mL to about 200 ug/mL.

20 69. The method of claim 68, wherein the molar ratio of Ca^{+2} to DNA-phosphate is about 3.

70. The method of claim 66, wherein the concentration of Ca^{+2} in millimolar units, is about $16 \cdot e^{(0.1386 \cdot t)}$, wherein t is the volume-percent of *tert*-butanol, and the counterion to the Ca^{+2} is chloride, and wherein the concentration of tert-butanol is from about 15% to about 35% by volume.

71. The method of claim 59, wherein the counterion to the divalent cation is chloride.

72. The method of claim 59, wherein the DNA has a negative zeta potential.

73. The method of claim 59, which further comprises removing water and the lyophilizable, water-miscible alcohol from the composition.

74. The method of claim 73, wherein the water and the lyophilizable, water-miscible alcohol are removed by lyophilization.

75. The method of claim 73 which further comprises spray-drying the composition.

76. The process of claim 59 wherein said toroids, rods and spheres are stable to
5 shear stress.